RCE/1617

#24

Patent
Attorney's Docket No. 003300-606

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of	**BOX: RCE**
Åke LINDAHL et al.	Group Art Unit: 1617
Application No.: 09/155,642	Examiner: Shengjun Wang
Filed: October 2, 1998	Confirmation No.: 8949
For: BIOLOGICALLY ACTIVE COMPOSITION	

REQUEST FOR CONTINUED EXAMINATION TRANSMITTAL LETTER

BOX RCE
Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Applicant(s) requests continued examination under 37 C.F.R. § 1.114 and enclose the [ ] $370.00 (279) [X] $740.00 (179) fee due under 37 C.F.R. § 1.17(e).

1. Applicant(s) previously submitted the following documents for which continued examination is requested:
   - [X] Consider the amendment(s)/reply under 37 C.F.R. § 1.116 previously filed on December 13, 2001.
   - [ ] Consider the arguments in the Appeal Brief or Reply Brief previously filed on _.
   - [ ] Other: _____.

2. The following documents are enclosed with this submission:
   - [X] Amendment/Reply.
   - [ ] Affidavit(s)/Declaration(s).
   - [ ] Information Disclosure Statement (IDS).
   - [ ] Other: _____.

3.
   - [ ] Small entity status is hereby claimed.
   - [X] No additional claim fee is required.
   - [ ] The fee is calculated below on the basis of the highest number of claims already paid for in this application prior to this submission:

06/12/2002 SDENBOB1 00000105 09155642
01 FC:179 740.00 OP

21839

(05/02)

CLAIMS					
	NO. OF CLAIMS	HIGHEST NO. OF CLAIMS THUS PAID FOR	EXTRA CLAIMS	RATE	FEE
Basic Fee					$740.00 (101)
Total Claims		MINUS 20 =		× $18.00 (103) =	
Independent Claims		MINUS 3 =		× $84.00 (102) =	
If multiple dependent claims are presented, add $280.00 (104)					
Total Fee					
If small entity status is claimed, subtract 50% of Total Fee					
TOTAL FEE DUE					**$740.00**

4. [X] A check in the amount of $ 740.00 is enclosed for the fee due.

5. [ ] Charge $ _____ to Deposit Account No. 02-4800 for the fee due.

6. [ ] Applicant(s) requests suspension of action by the Office until at least _, which does not exceed three months from the filing of this RCE, in accordance with 37 C.F.R. § 1.103(c). The required fee under 37 C.F.R. § 1.17(i) is enclosed.

The Commissioner is hereby authorized to charge any appropriate fees under 37 C.F.R. §§ 1.16, 1.17 and 1.21 that may be required by this paper, and to credit any overpayment, to Deposit Account No. 02-4800. This paper is submitted in duplicate.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

By: Jennifer Topmiller
Jennifer A. Topmiller
Registration No. 50,435

P.O. Box 1404
Alexandria, Virginia 22313-1404
(703) 836-6620

Date: June 11, 2002

Attorney's Docket No. 003300-506 Patent

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of	)	**BOX: RCE**
	)	
Ake LINDAHL *et al.*	)	Group Art Unit: 1617
	)	
Application No.: 09/155,642	)	Examiner: Shengjun Wang
	)	
Filed: October 2, 1998	)	Confirmation No: 8949
	)	
For: BIOLOGICALLY ACTIVE COMPOSITION	)	

REPLY PURSUANT TO 37 C.F.R. § 1.114

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Further to the Reply and Amendment filed December 13, 2001, requested to be entered in the Request for Continued Examination filed herewith, and in complete response to the Official Action mailed September 14, 2001, (Paper No. 18), and the Advisory Action mailed January 7, 2002, (Paper No. 20), Applicants submit the following remarks. A Petition for Extension of Time to respond after filing the Notice of Appeal on January 14, 2002, to extend the period for response from March 14, 2002, to June 14, 2002, is submitted in a separate paper filed herewith.

As correctly stated in the Office Action mailed September 14, 2001, but incorrectly stated in the Advisory Action mailed January 7, 2002, Claims 55-99 are pending in the present application. Claims 55-58, 61-79, 82, 85-94, and 97 stand rejected. Claims 59, 60, 80, 81, 83, 84, 95, 96, 98, and 99 stand withdrawn from consideration. Claim 97 was mistakenly identified as withdrawn from consideration in the Advisory Action. Claim 97

recites "wherein the steroid is a corticosteroid," the elected species, as noted by the Examiner in the Official Action mailed July 17, 2001, (Paper No. 16). Claim 97 depends from Claim 58, which is currently under consideration. Acknowledgment of the correct claims is respectfully requested.

Rejection Under 35 U.S.C. § 112, Second Paragraph

Claim 86 stands rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. The Examiner argues that the term "low" is not defined by the claim, nor by the specification. Without conceding the grounds of this rejection and solely in an effort to expedite prosecution, this language has been deleted from Claim 86 in the Amendment filed December 13, 2001, thereby mooting the rejection. The Examiner acknowledged that this amendment would overcome this rejection in the Advisory Action. Accordingly, withdrawal of this rejection is thus respectfully requested.

Rejections Under 35 U.S.C. § 103(a)

Claims 55-58, 61-79, 82, 85-94, and 97 stand rejected under 35 U.S.C. § 103(a) as purportedly unpatentable over Yamada *et al.* (U.S. Patent 5,362,497) in view of Wang *et al.* (U.S. Patent No. 4,299,828) and Cooper *et al.* (U.S. Patent No. 4,552,872). This rejection has been maintained by the Examiner in the Advisory Action mailed January 7, 2002. In the Office Action mailed April 17, 2001, (Paper No. 16), the Examiner argued that Yamada *et al.* disclose a transdermal therapeutic composition comprising a pharmaceutical active ingredient, a water-soluble absorption enhancer, a fat soluble

absorption enhancer comprising fatty alcohol, and a lower alchol ester of aliphatic carboxylic acid. The Examiner admitted that Yamada *et al.* do not expressly teach the particular formulation of the invention "which has corticosteroid as the active ingredient, and comprising unsaturated alcohols, lower alcohol ester of fatty acid, wax, and plasticizing oil with the particular percentage, or the particular form, stick, or the method of using the same." [See Official Action mailed April 17, 2001, pages 3-4]. However, the Examiner suggested that Cooper *et al.* disclose unsaturated alcohols are particularly useful in topical corticosteroid compositions and the inclusion of wax for stiffness. The Examiner further believes that Wang *et al.* disclose a corticosteroid stick formulation with wax. Thus, the Examiner surmised that one of "ordinary skill in the art would be motivated to modify the composition of Yamada to make a corticosteroid topical composition employing oleyl alcohol as the fat soluble enhancer and propylene glycol as the water soluble enhancer with the particular amounts claimed herein because both are known to be useful to enhance the absorption of active ingredients...The employment of wax and plasticizer to render the final product certain properties is seen to been within the skill of artisan." [See Official Action mailed April 17, 2001, pages 4-5]. In the Advisory Action mailed January 7, 2002, and in response to the December 13, 2001 amendment to Claim 55, the Examiner argued that Yamada disclose a homogeneous composition by suppressing separation. This rejection, to the extent that it applies to the claims as amended, is respectfully traversed.

In order to establish *prima facie* obviousness under 35 U.S.C. § 103, the cited reference or combination of references must teach or suggest every element of the claims with a reasonable expectation of success. Moreover, there must be motivation, outside of

Applicants' disclosure, to modify or combine the cited references. See M.P.E.P. § 2143 *et seq.*

Claim 55, as amended, explicitly recites "a solid, dermatological composition comprising a biologically active agent dissolved in a *homogeneous* carrier system." Applicants maintain their position that Yamada *et al.* is *irrelevant* to the presently claimed invention and, in fact, teaches away from the presently claimed invention. Yamada *et al.* describe the essence of their invention under the heading "Problems that the Invention is to Solve," column 2, lines 21-30. In this section, it is clearly stated that the invention of Yamada *et al.* is a way to avoid separation of a transdermal therapeutic composition, comprising a water-soluble and a lipid-soluble enhancer from an adhesive via the use of a water absorbent resin. Yamada *et al.* state that the use of alkylene glycol and fatty acids or alcohols are incompatible (col. 1, lines 62-66). Applicants invention solves the incompatibility problem via specific mixtures of solvents to create a one-phase system while the solution to the problem in Yamada *et al.* is a multi-phase system with a superabsorbent polymer. Applicants submit that the skilled artisan would not obviously appreciate that enhanced homogeneity and penetration could be generated by a formulation that does not contain adhesives and superabsorbing polymers such as those discussed by Yamada *et al.*

For the convenience of the Examiner, the differences between the Yamada *et al.* publication and the present invention are highlighted in the following table.

Component	**Yamada *et al.***	**Applicants' Invention**
Active Agent	YES	YES
Hydrophilic Enhancer	YES	YES*

Lipid Enhancer	YES	**
Superabsorbing Resin	YES	NO
Waxes	NO	YES
Plasticizer	NO	YES***
One-phase System	NO	YES
Multi-phase System	YES	NO
Solvent for Active Agent	-	YES

* - The solvent system of the presently claimed invention includes compounds that are regarded as water-soluble enhancers by Yamada *et al.* The present application demonstrates that the penetration enhancing effect of the presently claimed invention occurs when more than 12% of alkylene glycol is included in the formulation of the present invention. Alkylene glycol acts as the solvent for the active ingredient in the presently claimed invention. Yamada indicates that water-soluble enhancers are between 1 and 50%. In the current invention, alkylene glycol must be present in at least 12%. Moreover, it is impossible to include more than about 23% due to separation of the one-phase system of the present invention at higher concentrations.

** - The present invention contains a compound as the solvent for the active ingredient, whereas Yamada *et al.* use the compound as an enhancer.

*** - The addition of a plasticizer is an important feature of the present invention. The plasticizer softens the physical appearance and minimizes the occurrence of cracks in the stick preparations after packaging into solid composition containers.

Applicants respectfully submit that Yamada *et al.* do not disclose nor suggest that the incompatibility problem can be solved by a specific mixture of solvent in a wax-

containing matrix. Yamada *et al.* do not disclose nor suggest that this problem can be accomplished in a one-phase, water-free system nor that the physical properties of the invented formulation can be improved via the addition of a plasticizing oil. Yamada *et al.* do not disclose nor suggest the amounts of enhancer or solvent according to the presently claimed invention. The skilled artisan, upon reading the Yamada *et al.* publication would come to the conclusion that a satisfactory homogeneous composition in the absence of the superabsorbing resin, a critical component of Yamada *et al.*, could not be generated. In this sense, the Yamada *et al.* publication clearly teaches away from the present invention.

Applicants also maintain their argument that Cooper *et al.* teach away from the presently claimed invention. The Examiner's attention is directed to column 10, lines 35-54, wherein Cooper *et al.* specifically state that the use of hydrocarbons should be avoided or limited to not more than 10%, preferably not more than 5%. Applicants have discovered satisfactory delivery of the active ingredient in a composition that contradicts the teachings of Cooper *et al.* Cooper *et al.* also state that fatty alcohols should be avoided due to lowered absorption of the active ingredient and that the use of oils should preferably be limited to less than 0.5% (column 10, line 55, to column 11, lines 17), which is also in direct contrast to the claimed invention.

Applicants respectfully maintain that, even when considered together, the cited publications do not contain all the elements of the presently claimed invention. Further, Applicants have clearly demonstrated that both Yamada *et al.* and Cooper *et al.* teach away from, rather than disclose or suggest, the presently claimed invention and thus, there is no reasonable expectation of success. Applicants strongly disagree that the combination of the

Yamada *et al.* and Cooper *et al.* publications (in further combination with Wang *et al.*) would have thus motivated one skilled in the art to arrive at the present invention. Accordingly, Applicants submit that the presently claimed invention cannot be *prima facie* obvious over Yamada *et al.* in view of Wang *et al.* and Cooper *et al.* Withdrawal of this rejection is respectfully requested.

Conclusions

From the foregoing, further and favorable action in the form of a Notice of Allowance is respectfully requested and such action is earnestly solicited.

In the event that there are any questions concerning this amendment or the application in general, the Examiner is respectfully requested to telephone the undersigned so that prosecution of the application may be expedited.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

By: Jennifer Topmiller
Jennifer Topmiller, Ph.D.
Registration No. 50,435

P.O. Box 1404
Alexandria, Virginia 22313-1404
(703) 836-6620

Date: June 11, 2002